IN THE UNITED STATES DISTRICT COURT
FOR THE WESTERN DISTRICT OF PENNSYLVANIA

AMGEN INC. and AMGEN MANUFACTURING LIMITED, Plaintiffs, v. MYLAN INC., MYLAN PHARMACEUTICALS INC., MYLAN GMBH and MYLAN N.V., Defendants.	Civil Action No. 17-cv-01235-MRH *Electronically Filed* **REDACTED VERSION**

BRIEF IN SUPPORT OF MYLAN'S MOTION FOR JUDGMENT ON THE PLEADINGS PURSUANT TO RULE 12(c) REGARDING U.S. PATENT NO. 8,273,707

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Defendants Mylan Inc., Mylan Pharmaceuticals Inc., Mylan GmbH and Mylan N.V. (collectively, "Defendants" or "Mylan") move for dismissal of Plaintiffs Amgen Inc.'s and Amgen Manufacturing Limited's (collectively, "Amgen") allegations of infringement of the '707 patent because, under any reasonable interpretation, Mylan simply cannot infringe the '707 patent.

I. INTRODUCTION.

Amgen's '707 patent is drawn to a narrow process for purifying proteins that requires the use of one of three *particular* "salt pairs," yet Amgen insists on stretching the '707 patent beyond its limits in litigation—asserting infringement where, as a matter of law, it cannot succeed. Indeed, a Delaware Court has already dismissed litigation against a similarly-situated defendant—holding that Coherus Biosciences Inc. ("Coherus") cannot infringe the '707 patent as a matter of law (literally or under the doctrine of equivalents) precisely because Coherus does not use any of the *particular* salt pairs claimed. Judge Stark looked at the same evidence presented here and found that Amgen had clearly and unmistakably surrendered processes using combinations of salts different from the three, specific pairs claimed in the '707 patent and dismissed Amgen's infringement allegations. (*See* Section II.B. below). Amgen cannot change the scope of its claims in this case, thus dismissal is required here as well.

This case, just as *Coherus*, differs somewhat from traditional patent infringement litigation in that the infringement inquiry is based upon an alleged artificial act of infringement—namely that Mylan GmbH filed a Biologics License Application ("BLA") seeking U.S. Food and Drug Administration ("FDA") approval to market a biologic product that is biosimilar to Amgen's Neulasta® (pegfilgrastim) product. The '707 patent is directed to a specific protein purification step used during manufacture. There is no dispute (nor could there be) about what

Mylan does in its accused manufacturing step, which the BLA describes in detail, as required by FDA. Thus, the sole dispute is a legal one: can the patent's claims be read so broadly as a matter of law that they cover the accused manufacturing step described in Mylan's BLA?[1]

Just as in *Coherus*, the answer here is clearly no—the '707 patent requires a manufacturing process that uses one of three specific pairs of salts: citrate and sulfate; citrate and acetate; or acetate and sulfate. [redacted]

Amgen may nonetheless suggest that the arguments herein are somehow different than Coherus' or better suited to a later stage of the litigation, e.g., after claim construction or expert discovery. Not so. Dismissal at this early stage is entirely appropriate, particularly because these are issues of law and the parties' early exchange of information establishes there can be no infringement. Further, as in *Coherus*, no amount of discovery could change Amgen's (or the Court's) understanding of the accused process in any material way. Nor could any construction of the relevant claim terms possibly encompass the process described in Mylan's BLA.

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[1] It is Mylan's BLA that controls the infringement inquiry; the BLA must define the product and process that will be used for any approved product. *See, e.g.*, 42 U.S.C. § 262(*l*)(3)(A)(i); 35 U.S.C. § 271(e)(2)(C)(i) (filing a BLA "shall be an act of infringement"); *see also Bayer AG v. Elan Pharm. Research Corp.*, 212 F.3d 1241, 1248-50 (Fed. Cir. 2000) (finding an ANDA—similar to a BLA—defines the infringement inquiry).

[2] "Prosecution history estoppel applies as part of an infringement analysis to prevent a patentee from using the doctrine of equivalents to recapture subject matter surrendered from the literal scope of a claim during prosecution." *Trading Techs. Int'l, Inc. v. Open E Cry, LLC*, 728 F.3d 1309, 1322 (Fed. Cir. 2013).

[3] "M" refers to "molar" (or "moles per liter") which is a measure of concentration. One molar or "M" is equal to 1000 millimoles per liter, which is abbreviated as "mM." Thus 0.1 M is equivalent to 100 mM.

II. BACKGROUND.

The Biologics Prices Competition and Innovation Act ("BPCIA") provides a process for an applicant (here, Mylan GmbH) to obtain FDA approval to market a "biosimilar" drug product—i.e., one that is "highly similar" to an already-approved biologic product, known as the "reference product." *See* 42 U.S.C. §§ 262(i), (k). On December 9, 2016, Mylan GmbH submitted its BLA to FDA pursuant to 42 U.S.C. § 262(k), seeking approval of Pegfilgrastim (MYL-1401H) Solution for Subcutaneous Injection, a proposed biosimilar to Neulasta® (pegfilgrastim) ("Mylan's BLA"). (ECF No. 27, Mylan Answer, Defenses and Countercls. ¶ 33 (Nov. 22, 2016)).

The BPCIA also establishes a patent dispute resolution framework in which the parties exchange a significant amount of technical information and contentions prior to instigating any district court proceedings. *See* 42 U.S.C. § 262(*l*). Here, Mylan GmbH provided Amgen with its entire BLA and hundreds of pages of additional information regarding its manufacturing process pursuant to 42 U.S.C. § 262(*l*)(2)(A). (ECF No. 52, Amgen Answer to Mylan's Countercls. ¶ 34 (Jan. 5, 2018) ("Amgen Answer")). Mylan's BLA describes the proposed product that Mylan seeks FDA approval to market and the manufacturing process that Mylan told FDA it will use, and it must use, for the same. *See* 42 U.S.C. § 262(*l*)(2)(A). Amgen then identified patents for which it believed infringement "could reasonably be asserted" against Mylan, including the '707 patent. (Amgen Answer ¶¶ 42, 44). The parties exchanged infringement and invalidity contentions with respect to, among others, the '707 patent pursuant to 42 U.S.C. § 262(*l*)(3)(A)-(C). (*Id.* ¶¶ 43, 46-47). Despite Mylan's detailed contentions confirming non-infringement, Amgen chose to file suit based on Mylan's filing of its BLA. *See* 35 U.S.C. § 271(e)(2)(C)(i). Amgen alleges that Mylan's process for manufacturing its pegfilgrastim biosimilar infringes,

among others, the '707 patent. Amgen further seeks to enjoin Mylan from launching its pegfilgrastim biosimilar product. (ECF No. 1, Compl. ¶¶ 99-100 (Sept. 22, 2017) ("Compl.")).

A. The '707 Patent is Directed Toward an Allegedly Improved Protein-Purification Process Comprising a Particular Salt Combination.

As Judge Burke in Delaware found:

> [t]he '707 patent is directed to a process for purifying proteins. Its specification explains that biologic drug products constitute therapeutic proteins that are manufactured inside living cells. These proteins must then be separated from the source material. One such purification technique is known as hydrophobic interaction chromatography ("HIC").

(Ex. 1, R&R at 2[4] (citations omitted); *see also* Ex. 2, '707 patent at col. 1, ll. 19-51; *id.* at col. 3, ll. 53-54). HIC is a type of column chromatography in which

> a solution made up of the desired protein and associated impurities is poured onto a column filled with solid particles known as the "matrix." The interaction between the matrix material and loading solution causes the proteins to adhere to the matrix as the solution flows through the matrix. This step in the HIC process is known as "loading" the mixture onto the column. More solution is then poured through the column to "wash" it. Finally, a different solution is then poured through the column to "elute" the desired proteins therefrom.

(Ex. 1, R&R at 2 (citations omitted); *see also* Ex. 2, '707 patent at col. 1, ll. 40-49; *id.* at col. 3, ll. 53-61; *id.* at col. 4, ll. 27-30). Additionally, prior to loading, the matrix or stationary phase is prepared by equilibrating the column with a buffer solution (which does not contain the protein) to prepare the column for the load. (Ex. 2, '707 patent at col. 6, ll. 57-60).

This process is generally illustrated in the following, **Figure 1**:

[4] As explained in more detail below, on March 26, 2018, Chief Judge Stark adopted Magistrate Judge Burke's Report and Recommendation, and overruled Amgen's objections. (*See* Ex. 3, Mem. Order).

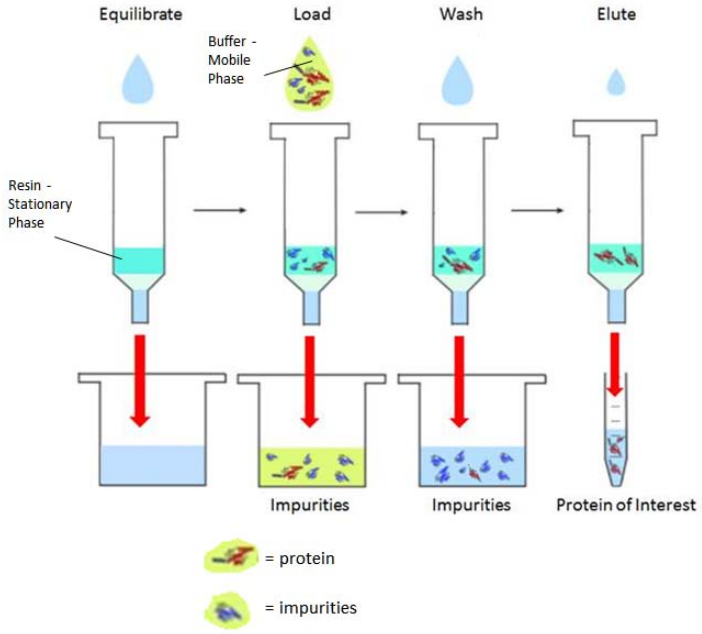

Figure 1

Sometimes, there is too much of the desired protein for all of it to stick to the matrix when loaded. As a result, significant amounts of the protein can be washed away with the impurities and lost before elution begins—a situation known as "breakthrough." (Ex. 2, '707 patent at col. 3, ll. 37-41; *id.* at col. 4, ll. 10-12). Amgen's alleged invention is a purported "solution" to the "problem with HIC known as 'breakthrough.'" (Ex. 3, R&R at 2-3). As Judge Burke explained:

> [t]he specification explains that the claimed process increases the "dynamic capacity" of the column by "increas[ing] . . . the amount of protein that can be loaded onto a column without 'breakthrough[.]'" It does so by using "intermediate concentration[s]" of a combination of salts in the loading solution.

(*Id.* at 3 (citations omitted); *see also* Ex. 2, '707 patent at col. 2, ll. 39-42 ("The two salt buffers of the present invention result in an increase in dynamic capacity of an HIC column for a particular protein compared with the dynamic capacity achieved by single salts"); *id.* at col. 3, ll. 37-40). Concentration is the amount of substance in a given volume of solvent or solution. As Judge Burke found:

> [a]ll 13 claims of the patent have at least two requirements. First, the combination of salts that is used in the loading solution must be one of three listed pairs of salts: "citrate and sulfate, citrate and acetate, [or] sulfate and acetate" (the "salt pairing limitation"). Second, the claims require that "the concentration of each of the first salt and the second salt in the mixture is between about 0.1 M and about 1.0."

(Ex. 3, R&R at 3 (citations omitted); *see also* Ex. 2, '707 patent at col. 15, ll. 15-18; *id.* at col. 16, ll. 15-18). The '707 patent also teaches that salt combinations other than these specific citrate/sulfate/acetate combos "did ***not*** increase the dynamic capacity" of the HIC column and "did ***not*** prove to be an effective combination," including because the low concentrations required to avoid breakthrough are "too low to improve dynamic capacity." (Ex. 2, '707 patent at col. 13, l. 64 – col. 14, l. 5 (emphasis added)).

Despite the focus of the claims of the '707 patent on the three particular salt pairs claimed, the specification discloses that "combining two different salts having different lyotrophic values with a protein preparation allows more protein to be loaded onto a column with no or negligible breakthrough compared with higher salt concentrations of each single salt." (Ex. 2, '707 patent at col. 4, ll. 47-52). The '707 patent further discloses (but does not claim) a list of "different salts," including [redacted]

[redacted]

(*Id.* at col. 4, ll. 33-46 (emphasis added)).

B. Amgen Clearly and Unmistakably Surrendered Prior Art Salt Combinations During Prosecution of the '707 Patent.

Before the Patent Office, Amgen made clear that use of the particular combinations of salts claimed, and their purported ability to increase a column's dynamic capacity, was what saved the claimed invention from being ruled unpatentable in light of the prior art. In October 2010, the Examiner rejected the claims of the '707 patent as obvious over U.S. Patent No. 5,231,178 to Holtz ("Holtz"), which the Examiner found disclosed a method for purifying insulin-like growth hormone using salts that improve the hydrophobic interaction of the protein, e.g., sodium sulfate, potassium sulfate, ammonium sulfate, potassium phosphate, sodium acetate, ammonium acetate, sodium chloride, sodium citrate and the like. (Ex. 4, '707 patent PH, 10/13/2010 Office Action at 4). The Examiner explained that:

> [i]t would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to purify a protein including an insulin-like growth hormone via the instantly claimed steps based upon the overall beneficial teachings provided by the cited reference. The adjustment of particular conventional working conditions (if not expressly taught) is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan.

(*Id.* at 5). Responding to the Office Action, Amgen argued that:

> the pending claims recite a particular *combination* of salts. No combinations of salts is taught nor suggested in the Holtz et al. patent, nor is the *particular* combinations of salts recited in the pending claims taught nor suggested in this reference.

(*Id.*, 1/26/2011 Resp. to Office Action at 5 (emphasis in original)). Amgen continued that "[t]he claimed subject matter is directed to use of combinations of salt that *increase the dynamic capacity* of the [HIC] columns." (*Id.*).

Amgen also submitted an inventor declaration that discussed the advantages of the three particular salt pairs claimed: "sulfate/citrate," "sulfate/acetate," and "acetate/citrate." The

declaration stated that "[u]se of *this particular combination of salts* greatly improves the cost-effectiveness of commercial manufacturing." (Ex. 4, '707 patent PH, 1/20/2011 Senczuk Decl. ¶ 4 (emphasis added)).

Amgen left no doubt that its claimed invention was limited to processes using the *particular* salt pairs claimed, and no others, in the load. In an April 2011 Office Action, the Examiner maintained his rejection of the claims as obvious over Holtz for the same reasons as described above. (Ex. 4, '707 patent PH, 4/7/2011 Office Action (Final Rejection) at 2-4). In response, Amgen *again* argued Holtz did not teach "the use of a *combination* of salts" disclosed in the alleged invention. (*Id.*, 8/22/2011 Amendment After Final Rejection at 5). Amgen explained that Holtz "does not teach each and every element of the claimed invention[,]" "namely" because it "simply does not disclose, suggest or contemplate any steps involving a combination of two salts for any purpose whatsoever." (*Id.*). Amgen again emphasized that it was three particular salt combinations that distinguished the claimed process, arguing that:

> merely adding a second salt to the traditional HIC process, as the Patent Office appears to suggest, will not produce applicants' claimed method. In fact, merely adding a second salt to the traditional HIC process will not even provide a working method; in this scenario the protein to be purified will precipitate out of solution and it will not be possible to load the protein onto the HIC column.

(*Id.* at 7).

Amgen also made clear during prosecution of the '707 patent's parent application that the alleged invention cannot contain more than two salts. At the time, the pending claims in the parent application contained exactly the same language as in the '707 patent claims—"mixing a preparation containing the protein with a combination of a first salt and a second salt." (Ex. 5, '581 parent application PH, 11/16/2007 Resp. to Office Action and Amendment at 3). The

Examiner rejected the claims as anticipated by Holtz, because Holtz includes an example containing a load solution of ammonium sulfate, sodium acetate, sodium phosphate and sodium chloride—four (4) salts. (*Id.*, 2/14/2008 Office Action at 2-3). In response, Amgen argued that:

> Holtz et al. . . . does not teach or suggest combining the protein to be purified ***with the particular combination of two salts*** . . . before loading the protein on the HIC column. Instead, a protein solution containing lower concentrations of sodium acetate and sodium phosphate, together with NaCl and a high concentration of ammonium sulfate (***four salts, not a combination of two salts as recited in the claimed method***), is loaded onto the HIC column.

(*Id.*, 7/14/2008 Resp. to Office Action and Amendment at 6 (emphasis added); *see also id.* at 6-7 (arguing a different method in Holtz that described the preparation of the protein in a solution with three salts—sodium acetate, phosphate and ammonium sulfate—was a "three salt combination instead of two salts")). Thus, to avoid a prior art reference, Amgen argued that a solution containing more than two salts could not be considered "a combination of two salts as recited in the claimed method." (*Id.* at 6).

Amgen further argued that the respective concentrations of the two salts were key aspects of the purported invention. Just as in the '707 patent, the parent application required that each salt has a lower concentration limit of "about 0.1 M." (Ex. 5, '581 parent application PH, 7/14/2008 Resp. to Office Action and Amendment at 3). In the same response, Amgen argued that salt present in a concentration of 40 mM or 0.04 M in Holtz was a "lower concentration[]" than the concentration claimed—"between about 0.1 M and 1.0 M." (*Id.* at 6). Amgen made the same argument with respect to a solution in Holtz containing 50 mM of each salt. (*Id.* at 7).

The patent-in-suit, meanwhile, ultimately issued with thirteen claims, of which claims 1 and 10 are the only independent claims, and each requires "a preparation containing the protein with a combination of a first salt and a second salt" and that the preparation or load solution

contain *a combination of salts*, either [1] citrate and sulfate, [2] citrate and acetate, or [3] sulfate and acetate. All other claims depend from claims 1 and 10. Thus, every claim in the '707 patent requires the use of those specific pairs of salts (and no more)—in the loading solution. Moreover, every claim requires that each salt be present at a concentration of "between about 0.1 M and about 1.0 M." The parent claims issued with the same requirement for a two salt combination and the same salt concentration limitation as claimed in the '707 patent. (*See* Ex. 6, '395 patent at col. 15, l. 17 – col. 16, l. 30). In fact, the claims of the '395 patent, which issued from the parent application of the '707 patent, are almost identical to the claims of the '707 patent except they claim a different salt pair—phosphate and citrate. Because Amgen separately patented a different salt pair, it confirms that the alleged invention is only directed to the *particular* salt pairs claimed and cannot encompass any other unrecited salt combinations.

C. The Related Coherus Litigation Confirms Amgen Surrendered Claim Scope During Prosecution.

On May 10, 2017, Amgen filed a complaint in Delaware, alleging Coherus' proposed Neulasta® biosimilar would infringe the '707 patent. (*See* Complaint, *Amgen Inc. v. Coherus Biosciences, Inc*., No. 17-546-LPS-CJB (D. Del. May 10, 2017)). Coherus filed a Motion to Dismiss for Failure to State a Claim on June 1, 2017, in which Coherus argued, among other things, that (i) its process does not use any of the salt pairs required by the claims and, most notably, (ii) Amgen was estopped from alleging infringement under the doctrine of equivalents against processes using other salts.

On December 12, 2017, Magistrate Judge Burke issued a Report and Recommendation recommending granting Coherus' Motion, finding prosecution history estoppel barred Amgen from asserting combinations of salts other than those claimed. Citing Amgen's own arguments

to the Patent Office, the court determined Amgen had "clearly and unmistakably—and indeed, repeatedly—indicated to competitors that it surrendered processes using combinations of salts different from the '*particular* combinations of salts recited in the [] claims[.]" (Ex. 1, R&R at 12). The court focused on arguments distinguishing its invention from the prior art, specifically Holtz, and found "Amgen surrendered any claim to a process that used other, unrecited salt combinations." (*Id.* at 13-14; *id.* at 16 ("the patentee explicitly argued (at some length) to the Examiner, in order to overcome the rejection based on Holtz, that its claimed invention was distinguishable from Holtz because of the claims' use of specific salt pairs")).

Chief Judge Stark then, on March 26, 2018, overruled Amgen's objections and adopted Judge Burke's Report and Recommendation, ordering dismissal of Amgen's Complaint against Coherus on the '707 patent. (Ex. 3, Mem. Order at 2). Additionally, Judge Stark "agree[d] with Coherus that another reason Amgen's claim for infringement of the '707 patent must be dismissed is that the patentee dedicated to the public" salts alleged to be equivalent by disclosing the same in the '707 patent and failing to claim such salts. (*Id.* at 6-7).

D. Mylan's Manufacturing Process.

Mylan GmbH's BLA seeks approval of Pegfilgrastim (MYL-1401H) Solution for Subcutaneous Injection, a proposed biosimilar to Neulasta® (pegfilgrastim). Pegfilgrastim is a PEGylated form[5] of the recombinant human granulocyte colony-stimulating factor (GCSF) analog known as "filgrastim." Mylan manufactures filgrastim using [redacted]

[5] PEGylation is the process of binding a biodegradable polymer to a protein (here, filgrastim) that occurs *post*-purification and therefore is not relevant to the '707 patent. PEGylated filgrastim experiences increased retention time in the bloodstream. [redacted]

[redacted]

[redacted] (*See* Ex. 8, Amgen Contentions, App. A at 1).

1. [redacted]

[redacted] This is illustrated in the following **Figure 2:**

[redacted]

[redacted]

2. [redacted]

[redacted]

When a solution is diluted, the volume increases, and thus the concentrations of the component substances may change. For example, as illustrated in **Figure 3** below, when a solution is diluted by adding solvent but the amount of salt remains the same, the concentration of the salt is lowered when the volume of the solution increases:

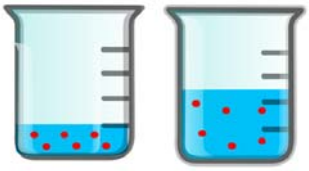

Figure 3

[redacted]

[redacted] (*See* Ex. 9, Amgen Statement Under 42 U.S.C. § 262(*l*)(3)(C) at 34-35; Ex. 8, Amgen Contentions, App. A at 1).[7]

III. ARGUMENT.

A. Governing Law.

A motion for judgment on the pleadings under Federal Rule Civil Procedure 12(c) may be granted when the movant clearly establishes that no material issue of fact remains to be resolved and that it is entitled to judgment as a matter of law. *Wiseman Oil Co., Inc. v. TIG Ins. Co.*, 878 F. Supp. 2d 597, 600 (W.D. Pa. 2012) (citing *Rosenau v. Unifund Corp*., 539 F.3d 218, 221 (3d Cir. 2008)). When reviewing a motion for judgment on the pleadings, "a court must view the facts in the plaintiff's complaint as true and draw all reasonable inferences in the plaintiff's favor." *Snyder v. Daugherty*, 899 F. Supp. 2d 391, 400 (W.D. Pa. 2012); *see also Fowler v. UPMC Shadyside*, 578 F.3d 203, 210-11 (3d Cir. 2009). In other words, a court applies the same standard to a 12(c) motion as a motion to dismiss pursuant to Rule 12(b)(6), except a Rule 12(c) motion can be made after the pleadings are closed. *Snyder*, 899 F. Supp. 2d at 400; *Pa. Gen. Energy Co. v. Grant Twp.*, 139 F. Supp. 3d 706, 711 (W.D. Pa. 2015); *Drennen v. Cmty. Bank of N. Va.*, No. 05-1386, 2009 WL 440960, at *2 n.1 (W.D. Pa. Feb. 23, 2009) (citing *Turbe v. Gov't of the V.I.*, 938 F.2d 427, 428 (3d Cir. 1991)).

Thus, the same analysis a court conducts under a motion to dismiss is appropriate. First, the court must separate the factual and legal elements of the claim, and "accept all of the complaint's well-pleaded facts as true, but may disregard any legal conclusions." *Fowler*, 578

[7] [redacted]

F.3d at 210-11. Second, the court must determine "whether the facts alleged in the complaint are sufficient to show that the plaintiff has a 'plausible claim for relief.'" *Id.* at 211 (quoting *Ashcroft v. Iqbal*, 556 U.S. 662, 679 (2009)). A plausible claim requires more than merely alleging entitlement to relief, rather it must "'show' such an entitlement with its facts." *Id.* (citing *Phillips v. Cty. of Allegheny*, 515 F.3d 224, 234-35 (3d Cir. 2008)). Therefore, a claimant's "obligation to provide the 'grounds' of his 'entitle[ment] to relief' requires more than labels and conclusions, and a formulaic recitation of the elements of a cause of action will not do." *Bell Atl. Corp. v. Twombly*, 550 U.S. 544, 555 (2007); *Iqbal*, 556 U.S. at 678.

In resolving a 12(c) motion, a court may consider, not only the pleadings, but also "undisputedly authentic documents attached to or submitted with the Complaint, as well as evidence outside the complaint/other items of record," including documents integral to or explicitly relied upon in the Complaint. *Wiseman*, 878 F. Supp. 2d at 601; *see also In re Burlington Coat Factory Secs. Litig.*, 114 F.3d 1410, 1426 (3d Cir. 1997); *Oshiver v. Levin, Fishbein, Sedran & Berman*, 38 F.3d 1380, 1384-85 & n.2 (3d Cir. 1994).

There is no question Mylan's BLA is the document that forms the basis of Amgen's Complaint and is thus "integral to the Complaint and one that the Court can rely upon at this stage." *See, e.g.*, *AstraZeneca Pharm. LP v. Apotex Corp.*, 669 F.3d 1370, 1378 n.5 (Fed. Cir. 2012) (finding that the district court did not err in considering defendant's submissions to the FDA in resolving a motion to dismiss, as the complaints at issue "referenced and relied on" those submissions); (*see also* Ex. 1, R&R at 6 n.6). When infringement turns on the contents of an FDA application (such as an ANDA or a BLA) courts may grant Rule 12 motions if what is required in the FDA application would not infringe. *AstraZeneca*, 669 F.3d at 1378 n.5.

A court may also consider the prosecution history of the patent-in-suit. *See Genetic Techs. Ltd. v. Bristol-Myers Squibb Co*., 72 F. Supp. 3d 521, 526 (D. Del. 2014) (finding motion "may also take judicial notice of the prosecution histories, which are 'public records'"); *Int'l Bus. Machs. Corp. v. Priceline Grp. Inc.*, No. 15-137-LPS-CJB, 2016 WL 626495, *20 n.18 (D. Del. Feb. 16, 2016); *Quest Integrity USA, LLC v. Clean Harbors Indus. Servs., Inc.*, Nos. 14-1482-SLR, 14-1483-SLR, 2015 WL 4477700, *1 n.4 (D. Del. July 22, 2015) (prosecution history "is a public document that the court may rely upon in deciding this motion to dismiss").

B. The Complaint Fails To State A Claim For Infringement.

As explained above, Amgen alleges Mylan's [redacted] infringes. For that process to infringe, [redacted] Amgen cannot prove either element as a matter of law. [redacted]

Separately, Amgen's specious argument that [redacted] could somehow infringe must also fail. (Ex. 9, Amgen Statement Under 42 U.S.C. § 262(*l*)(3)(C) at 35; Ex. 8, Amgen Contentions, App. A at 2-3). [redacted] Therefore, Mylan's accused process cannot infringe the '707 patent claims.

1. [redacted]

Mylan's process cannot literally infringe because [redacted]—is not "selected from the group consisting of [1] citrate and sulfate, [2] citrate and acetate, and [3] sulfate and acetate"—a limitation of both independent claims of the '707 patent. (Ex. 2, '707 patent at col. 15, ll. 14-16; *id*. at col. 16, ll. 14-16). For that reason alone, Mylan's process cannot literally infringe any asserted claim. Amgen admits as much, instead attempting to argue Mylan's process infringes the claims under the doctrine of equivalents.

As a matter of law, Amgen is estopped from making a doctrine of equivalents claim with respect to the [redacted] The Delaware Court agreed. That is because during prosecution of the '707 patent,

> Amgen distinguished a prior art reference ("Holtz") and overcame the patent examiner's [] rejection, on the ground that Holtz did not teach or suggest ***the particular combinations of salts*** (citrate/sulfate, citrate/acetate and sulfate/acetate) claimed in the patent. As such, . . . Amgen is now estopped from asserting that a different salt combination . . . is infringing.

(Ex. 1, R&R at 9 (emphasis added)). Indeed, "as if to highlight this point even further, so that the Examiner would not miss it, [Amgen] actually placed the word 'particular' in the phrase 'particular combination of salts' in italics." (*Id.* at 13 n.9).

Amgen didn't just argue its invention was the use of any combination of salts, but instead:

> distinguished its invention not only on that ground, but also for the independent reason that the invention recited the use of *particular* combinations of salts. And the patentee supported its position with an inventor declaration providing test results for those *particular claimed combinations*—one that touted the benefits of use of those specific combinations—in order to show how their use resulted in a process that improved the dynamic capacity of a HIC column.

(Ex. 1, R&R at 12-13 (footnote omitted)).

Having secured issuance by arguing the claims required the use of *specific* salt pairs, Amgen cannot now expand the scope of those claims to cover purported equivalents [redacted] Whether prosecution history estoppel applies, and therefore whether a patentee may assert the doctrine of equivalents for a particular claim limitation, is a question of law. *Spectrum Pharm., Inc. v. Sandoz Inc*., 802 F.3d 1326, 1337 (Fed. Cir. 2015). Prosecution history estoppel can occur in two ways: (1) by making a narrowing amendment to a claim ("amendment-based"); or (2) by surrendering claim scope through argument to the patent examiner ("argument-based"). *Conoco, Inc. v. Energy & Envtl. Int'l, L.C*., 460 F.3d 1349, 1363 (Fed. Cir. 2006); *see also Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., Ltd.*, 535 U.S. 722, 735, 739-40 (2002).

Here, Amgen cannot escape its argument-based estoppel. For argument-based estoppel to apply, "the prosecution history must evince a clear and unmistakable surrender of subject matter." *Conoco, Inc.*, 460 F.3d at 1364. The relevant inquiry is an objective test, which inquires "whether a competitor would reasonably believe that the applicant had surrendered the relevant subject matter." *Id.*; *see also AquaTex Indus., Inc. v. Techniche Sols.*, 419 F.3d 1374, 1382 (Fed. Cir. 2005). Even when "not necessary to secure allowance of the claim, statements that clearly and unmistakably surrender claim scope can preclude an assertion of equivalency." (Ex. 1, R&R at 9 n.7 (citing *Bayer*, 212 F.3d at 1252)).

There is no question that Amgen has done so here. By arguing "repeatedly" that the *particular* combination of salts (citrate/sulfate, citrate/acetate and sulfate/acetate) claimed by the '707 patent distinguished the invention from the prior art, Amgen "clearly and unmistakably . . .

indicated to competitors that it surrendered processes using combinations of salts different from the '*particular* combinations of salts recited in the [] claims[.]" (Ex. 1, R&R at 12).

As in *Coherus*, Amgen's attempted reliance on the doctrine of equivalents is barred for a further reason too—namely, the dedication-disclosure rule. (Ex. 3, Mem. Order at 6-7). Under that rule, when a patentee "discloses but declines to claim subject matter," it necessarily "dedicates that unclaimed subject matter to the public" and places it beyond the reach of the doctrine of equivalents. *Johnson & Johnston Assocs., Inc. v. R.E. Serv. Co.*, 285 F.3d 1046, 1054 (Fed. Cir. 2002). Here, Amgen disclosed the use of [redacted] "as useful for purifying proteins using HIC columns" yet failed to claim [redacted] in any of the listed salt pairs. (*See* Ex. 2, '707 patent at col. 3, ll. 22-24). Additionally, during prosecution of the '707 patent parent application, Amgen attempted to claim a process containing a first and second salt and argued that the specification (the same specification as the '707 patent) disclosed a number of different "potential salts" for the invention, including [redacted] (Ex. 5, '581 parent application PH, Original Claims; *id.*, 11/16/2007 Resp. to Office Action and Amendment at 6 (identifying "potential salts")). However, Amgen was forced to narrow its claims in the parent application to a combination of citrate and phosphate and failed to claim [redacted], thus dedicating it to the public, twice.

2. [redacted]

Nor can Amgen save its infringement allegations by looking at other steps in Mylan's process. [redacted]

[redacted], as required by the claims and thus as a matter of law cannot be used to attempt to show infringement of the '707 patent claims. Regardless, even if [redacted]—which Amgen is estopped from arguing is equivalent to the claimed pair.

First, any salt in [redacted] because the claims require mixing the salts with the protein ***prior to loading on the column***. Claim 1 states that the process comprises "*mixing* a preparation containing the protein with a combination of a first salt and a second salt, *loading the mixture* onto a hydrophobic interaction chromatography column." (Ex. 2, '707 patent at col. 15, ll. 11-14 (emphasis added)). Similarly, Claim 10 states that the process comprises "*mixing* a preparation containing the protein with a combination of a first salt and a second salt, and *loading the mixture* onto a hydrophobic interaction chromatography column." (*Id.* at col. 16, ll. 11-14 (emphasis added)). In each instance, the salt pair must be mixed with the protein preparation ***before*** the mixture is loaded onto the column.[8] *Mformation Techs., Inc. v. Res. In Motion Ltd.*, 764 F.3d 1392, 1398 (Fed. Cir. 2014). Amgen confirmed as much during prosecution of the '707 patent parent application, where Amgen argued that the exact same language regarding the mixing of the salt pair with the protein referred to mixing "***before loading the protein on the HIC column***." (Ex. 5, '581 parent application PH, 7/14/2008 Resp. to Office Action and Amendment at 6 (emphasis added)). Conversely, the equilibration buffer runs through the column *prior* to the load in order to prepare or "equilibrate" the column. The equilibration buffer is never mixed with the load containing the protein. Similarly, the wash buffer flows through the column *after*

[8] Consciously attempting to avoid this issue, Amgen alleges in its Complaint that "a preparation containing protein ***becomes*** mixed with a first salt and a second salt"—demonstrating Amgen knows there is no infringement of the claims. (*See, e.g.*, Compl. ¶ 90).

the load, to wash away any remaining impurities from the column. Common sense alone dictates that salts running through the column during equilibration or wash—and which are not mixed with the protein prior to loading—cannot satisfy the claimed salt pair limitation.

Second, even if any salt that runs through the column during equilibration or wash were relevant to the infringement analysis (it is not), prosecution history estoppel (which is a question of law) bars Amgen from asserting infringement.[9] [redacted], which if ever mixed [redacted] as required by the claims of the '707 patent, would constitute [redacted]. As detailed above, Amgen argued in response to a rejection over the prior art that "Holtz et al. . . . does not teach or suggest combining the protein to be purified with the particular ***combination of two salts, citrate and phosphate salts***" and went on to explain that the example in Holtz instead contained "***four salts***, not a combination ***of two salts*** as recited in the claimed method." (Ex. 5, '581 parent application PH, 7/14/2008 Resp. to Office Action and Amendment at 6 (emphasis added); *see also* Ex. 1, R&R at 10 n.8 (citing the same); Section II.B. above). Amgen's argument explicitly disclaimed solutions that contain more salts than the two-salt system that it alleges distinguishes its invention from the prior art.

The fact that Amgen made this argument during prosecution of the parent of the '707 patent—rather than the '707 patent itself—does not undermine this conclusion. It is well-settled

[9] "[W]here a patent applicant sets forth multiple bases to distinguish between its invention and the cited prior art, the separate arguments [can] create separate estoppels as long as the prior art was not distinguished based on the combination of these various grounds." *PODS, Inc. v. Porta Stor, Inc.*, 484 F.3d 1359, 1367 (Fed. Cir. 2007) (internal quotation marks and citation omitted).

that "prosecution disclaimer may arise from disavowals made during the prosecution of ancestor patent applications." *Ormco Corp. v. Align Tech., Inc*., 498 F.3d 1307, 1314 (Fed. Cir. 2007) (quoting *Omega Eng'g, Inc. v. Raytek Corp.*, 334 F.3d 1314, 1333 (Fed. Cir. 2003)). The question is whether the statements from the prosecution "relat[e] to the same subject matter as the claim language at issue in the patent being construed." (*Id.*). Here, the statements do not just relate to the same subject matter—the claim language at issue from the prosecution of the '581 parent application is identical to the language of the '707 patent.[10]

3. [redacted]

Even if the salts present in [redacted]—were somehow deemed sufficient to satisfy the salt pair limitation of the claims, there still can be no infringement because, [redacted] The claims require that the concentration of each of the loading mixture's two salts "is between about 0.1 M and about 1.0 M." (Ex. 2, '707 patent at col. 15, l. 18; *id.* at col. 16, l. 18). Thus, the minimum concentration required for infringement is "about 0.1 M" or 100

[10] (*See, e.g.*, Ex. 5, '581 parent application PH, 7/14/2008 Resp. to Office Action at 3 (claim for "A process for purifying a protein on a hydrophobic interaction chromatography column comprising ***mixing a preparation containing the protein with a combination of a first salt and a second salt***, loading the mixture onto a hydrophobic interaction chromatography column, and eluting the protein, where the first and second salts are citrate and phosphate salts, and wherein the concentration of each of the first salt and the second salt in the mixture is between about 0.1 M and about 1.0 [M]" (emphasis added)); *id*. at 4 (claim for "A method of increasing the dynamic capacity of a hydrophobic interaction chromatography column for a particular protein, comprising ***mixing a preparation containing the protein with a combination of a first salt and a second salt***, and loading the mixture onto a hydrophobic chromatography column, wherein the first and second salts are citrate and phosphate salts, and wherein the concentration of each of the first and second salts in the mixture is between about 0.1 M and about 1.0 M" (emphasis added)), *compare with* Ex. 2, '707 patent at claim 1 ("A process for purifying a protein on a hydrophobic interaction chromatography column such that the dynamic capacity of the column is increased for the protein comprising ***mixing a preparation containing the protein with a combination of a first salt and a second salt***, loading the mixture onto a hydrophobic interaction chromatography column, and eluting the protein, wherein the first and second salts are selected from the group consisting of citrate and sulfate, citrate and acetate, and sulfate and acetate, respectively, and wherein the concentration of each of the first salt and the second salt in the mixture is between about 0.1 M and about 1.0.") (emphasis added)).

mM. According to Amgen, [redacted] (*See* Ex. 9, Amgen Statement Under 42 U.S.C. § 262(*l*)(3)(C) at 34-35).

No plausible construction of "about 0.1 M" could stretch the lower boundary of the claimed concentration range [redacted][11] Still, there is no need to determine exactly how much flexibility "about" provides—because Amgen surrendered any claim to processes using salt concentrations as low [redacted]. As explained above, the '707 patent parent application contains identical claim language that sets "about 0.1 M" as the lower limit of each salt's concentration in the loading mixture. (Ex. 5, '581 parent application PH, 4/13/2007, Resp. to Restriction Requirement at 3). In response to a prior art rejection, Amgen argued that the prior art's salt concentrations—acetate and phosphate salts at 0.04 M (or 40 mM)—were below the claimed range of "about 0.1 M to about 1.0 M." (*Id.*, 7/14/2008 Resp. to Office Action at 6).

By arguing that a concentration of 0.04 M was below the range of "about 0.1 M to about 1.0 M," Amgen necessarily disclaimed processes using even lower concentrations, [redacted].[12] When an applicant secures a patent by arguing that the claims do not encompass certain subject matter, it cannot later assert the contrary. *See, e.g.*, *Chimie v. PPG Indus.*, 402 F.3d 1371, 1384 (Fed. Cir. 2005). Here, because

[11] [redacted]

[12] Moreover, Amgen's disclaimer of processes employing lower concentrations of salts is consistent with its statements regarding the invention in an opposition filed in a related European patent ("EP '512"). (*See, e.g.*, Ex. 10, EP '512 PH, 6/25/2013 Patentee Submission at 3 (arguing a concentration of 40 mM or 50 mM is "outside the claimed range" and "not within the scope of the claim and … beyond the understanding of the skilled person")). EP '512 claims priority to the same PCT application as the '707 patent. Amgen's "admissions" are consistent with the claims and the specification of the '707 patent. *Apple Inc. v. Motorola, Inc.*, 757 F.3d 1286, 1313 (Fed. Cir. 2014), *overruled on other grounds by Williamson v. Citrix Online, LLC*, 792 F.3d 1339 (Fed. Cir. 2015).

Amgen secured its patent by arguing that 0.04 M was below "about 0.1 M," it has disclaimed any argument that even lower concentrations literally infringe.

As explained above, arguments made during prosecution of the parent of the '707 patent are equally relevant, particularly where the claim language is exactly the same as here. Thus, Amgen is estopped from resorting to the doctrine of equivalents to argue that [redacted] "is equivalent to a concentration within the claimed range." (Compl. ¶ 90). Amgen's arguments during prosecution estop it from arguing that concentrations below 0.04 M are equivalent to the claimed lower limit of "about 0.1 M." *Bayer*, 212 F.3d at 1253; (*see also* Ex. 1, R&R at 8-9; Ex. 3, Mem. Order at 5-6).

IV. CONCLUSION.

Mylan's BLA describes its manufacturing process in sufficient detail to establish, as a matter of law, that there can be no infringement. [redacted], and Amgen is estopped from relying on the doctrine of equivalents to try to satisfy those limitations. And it is Mylan's BLA that controls the infringement inquiry, it defines the product and process that will be used for any approved product. *See, e.g.*, 42 U.S.C. § 262(*l*)(3)(A)(i). Mylan cannot market a pegfilgrastim product manufactured in a manner that is different from what the BLA describes.

Finally, no construction of the relevant claim terms could possibly encompass the process described in Mylan's BLA. (*See* Ex. 1, R&R at 15 (finding Amgen failed to explain "how claim construction or discovery would shed light on the objective inquiry regarding whether argument-based prosecution history estoppel applies"); Ex. 3, Mem. Order at 7 (same)). That much is clear not only from the claim language but also from Amgen's arguments during prosecution—as described in detail above. Similar to the court's finding in *Coherus*, "there is no plausible claim

that [Mylan's] process satisfies the salt pairing limitation," (Ex. 1, R&R at 5), or that Mylan's process satisfies the concentration limitations of the claims of the '707 patent.

Thus, for at least the reasons described above, Mylan's motion for judgment on the pleadings should be granted.

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Respectfully submitted,

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